

CLAIMS

What is claimed is:

1. A method of identifying a region of a genome of a cell to which a protein of interest binds, comprising the steps of:
 - a) crosslinking DNA binding protein in the cell to genomic DNA of the cell, thereby producing DNA binding protein crosslinked to genomic DNA;
 - b) generating DNA fragments of the genomic DNA crosslinked to DNA binding protein in a), thereby producing a mixture comprising DNA fragments to which DNA binding protein is bound;
 - c) removing a DNA fragment to which the protein of interest is bound from the mixture produced in b);
 - d) separating the DNA fragment identified in c) from the protein of interest;
 - e) amplifying the DNA fragment of d);
 - f) combining the DNA fragment of e) with DNA comprising a sequence complementary to genomic DNA of the cell, under conditions in which hybridization between the DNA fragment and a region of the sequence complementary to genomic DNA occurs; and
 - g) identifying the region of the sequence complementary to genomic DNA of f) to which the DNA fragment hybridizes,whereby the region identified in g) is the region of the genome in the cell to which the protein of interest binds.
2. The method of Claim 1 wherein the cell is a eukaryotic cell.
3. The method of Claim 1 wherein the protein of interest is selected from the group consisting of: a transcription factor and an oncogene.

4. The method of Claim 1 wherein the DNA binding protein of the cell is crosslinked to the genome of the cell using formaldehyde.
5. The method of Claim 1 wherein the DNA fragment of c) to which is bound the protein of interest is identified using an antibody which binds to the protein of interest.
6. The method of Claim 1 wherein the DNA fragment of e) is amplified using ligation-mediated polymerase chain reaction.
7. The method of Claim 1 wherein the complement sequence of the genome of f) is a DNA microarray.
8. The method of Claim 1 further comprising:
 - h) comparing the region identified in g) with a control.
9. A method of identifying a region of a genome of a cell to which a protein of interest binds, comprising the steps of:
 - a) formaldehyde crosslinking DNA binding protein in the cell to genomic DNA of the cell, thereby producing DNA binding protein crosslinked to genomic DNA;
 - b) generating DNA fragments of the genomic DNA crosslinked to DNA binding protein in a), thereby producing DNA fragments to which DNA binding protein is bound;
 - c) immunoprecipitating the DNA fragment produced in b) to which the protein of interest is bound using an antibody that specifically binds the protein of interest;
 - d) separating the DNA fragment identified in c) from the protein of interest;

- e) amplifying the DNA fragment of d) using ligation-mediated polymerase chain reaction;
- f) fluorescently labeling the DNA fragment of e);
- g) combining the labeled DNA fragment of e) with a DNA microarray comprising a sequence complementary to genomic DNA of the cell, under conditions in which hybridization between the DNA fragment and a region of the sequence complementary to genomic DNA occurs;
- h) identifying the region of the sequence complementary to genomic DNA to which the DNA fragment hybridizes by measuring the fluorescence intensity; and
- i) comparing the fluorescence intensity measured in h) to the fluorescence intensity of a control,

whereby fluorescence intensity in a region of the genome which is greater than the fluorescence intensity of the control in the region indicates the region of the genome in the cell to which the protein of interest binds.

10. A method of determining a function of a protein of interest which binds to a genome of a cell, comprising the steps of:
 - a) crosslinking DNA binding protein in the cell to genomic DNA of the cell, thereby producing DNA binding protein crosslinked to genomic DNA;
 - b) generating DNA fragments of the genomic DNA crosslinked to DNA binding protein in a), thereby producing a mixture comprising DNA fragments to which DNA binding protein is bound;
 - c) removing the DNA fragment to which the protein of interest is bound from the mixture produced in b);
 - d) separating the DNA fragment identified in c) from the protein of interest;
 - e) amplifying the DNA fragment of d);

- f) combining the DNA fragment of e) with DNA comprising a sequence complementary to genomic DNA of the cell, under conditions in which hybridization between the DNA fragment and a region of the sequence complementary to genomic DNA occurs;
 - g) identifying the region of the sequence complementary to genomic DNA of f) to which the DNA fragment hybridizes; and
 - h) characterizing the region identified in g),
- wherein the characteristics of the region of h) indicates a function of the protein of interest which binds to the genome of the cell.

11. A method of determining whether a protein of interest which binds to the genome of a cell functions as a transcription factor, comprising the steps of:
- a) crosslinking DNA binding protein in the cell to the genomic DNA of the cell, thereby producing DNA binding protein crosslinked to genomic DNA;
 - b) generating DNA fragments of the genomic DNA crosslinked to DNA binding protein in a), thereby producing a mixture comprising DNA fragments to which DNA binding protein is bound;
 - c) removing the DNA fragment to which the protein of interest is bound from the mixture produced in b);
 - d) separating the DNA fragment identified in c) from the protein of interest;
 - e) amplifying the DNA fragment of d);
 - f) combining the DNA fragment of e) with DNA comprising a sequence complementary to genomic DNA of the cell, under conditions in which hybridization between the DNA fragment and a region of the sequence complementary to genomic DNA occurs; and
 - g) identifying the region of the sequence complementary to genomic DNA of f) to which the DNA fragment hybridizes,

wherein if the region of the sequence complementary to genomic DNA of g) is a regulatory region, then the protein of interest is a transcription factor.

12. A method of identifying a set of genes, the members of which are genes for which cell cycle regulator binding correlates with gene expression, comprising:
 - (a) identifying a set of genes that is bound in vivo by at least one cell cycle regulator in a selected cell type;
 - (b) comparing the set of genes identified in (a) with genes whose expression levels vary in a periodic manner during the cell cycle of the selected cell type; and
 - (c) identifying genes that are bound by one or more of the cell cycle regulators, thus identifying a set of genes, the members of which are genes whose expression levels vary in a periodic manner during the cell cycle and are bound by at least one cell cycle regulator, wherein the set identified in (c) is referred to as a set of genes, the members of which are genes for which cell cycle regulator binding correlates with gene expression.
13. The method of claim 12, wherein the selected cell type is a yeast cell.
14. The method of claim 13, wherein the at least one cell cycle regulator is at least one of the nine known yeast cell cycle transcriptional activators.